CLAIMS

We claim:

1. An isolated polypeptide of at least 15 amino acid residues comprising an epitope-bearing portion of a protein of SEQ ID NO:2 or SEQ ID NO:43.

2. The isolated polypeptide according to claim 1 wherein said polypeptide is selected from the group consisting of:

residues 15-163 of SEQ ID NO:2;
residues 46-163 of SEQ ID NO:2;
residues 15-170 of SEQ ID NO:2;
residues 46-170 of SEQ ID NO:2;
residues 15-234 of SEQ ID NO:2;
residues 46-234 of SEQ ID NO:2;
residues 15-229 amide of SEQ ID NO:2;
residues 15-230 of SEQ ID NO:2;
residues 15-345 of SEQ ID NO:2;
residues 46-345 of SEQ ID NO:2;
residues 164-345 of SEQ ID NO:2;
residues 235-345 of SEQ ID NO:2; and
residues 226-345 of SEQ ID NO:2.

3. An isolated polypeptide comprising a sequence of amino acids of the formula $R1_x$-$R2_y$-$R3_z$, wherein:

R1 comprises a polypeptide of from 100 to 120 residues in length that is at least 90% identical to residues 46-163 of SEQ ID NO:2, and comprises a sequence motif C[KR]Y[DNE][WYF]X{11,15}G[KR][WYF]C (SEQ ID NO:4) corresponding to residues 104-124 of SEQ ID NO:2;

R2 is a polypeptide at least 90% identical to residues 164-234 of SEQ ID NO:2;

R3 is a polypeptide at least 90% identical in amino acid sequence to residues 235-345 of SEQ ID NO:2 and comprises cysteine residues at positions corresponding to residues 250, 280, 284, 296, 335, and 337 of SEQ ID NO:2; a glycine residue

at a position corresponding to residue 282 of SEQ ID NO:2; and a sequence motif CX{18,83}CXGXCX{6,33}CX{20,40}CXC (SEQ ID NO:3) corresponding to residues 250-337 of SEQ ID NO:2; and

each of x, y, and z is individually 0 or 1, subject to the limitations that:

at least one of x and z is 1; and

if x and z are each 1, then y is 1.

4. The isolated polypeptide of claim 3 wherein x=1.

5. The isolated polypeptide of claim 4 wherein R1 comprises residues 46-163 of SEQ ID NO:2.

6. The isolated polypeptide of claim 4 wherein R1 is at least 90% identical to residues 18-163 of SEQ ID NO:2.

7. The isolated polypeptide of claim 4 wherein y=1.

8. The isolated polypeptide of claim 7 wherein z=1.

9. The isolated polypeptide of claim 3 wherein said polypeptide comprises residues 46-229 of SEQ ID NO:2, residues 164-345 of SEQ ID NO:2, or residues 46-345 of SEQ ID NO:2.

10. The isolated polypeptide of claim 3 wherein z=1.

11. The isolated polypeptide of claim 10 wherein R3 comprises residues 235-345 of SEQ ID NO:2.

12. The isolated polypeptide of claim 10 wherein y=1.

13. The isolated polypeptide of claim 12 wherein x=1.

14. The isolated polypeptide of claim 10, further comprising cysteine residues at positions corresponding to residues 286, 287, 291, and 294 of SEQ ID NO:2.

15. The isolated polypeptide of claim 3, further comprising an affinity tag.

16. The isolated polypeptide of claim 3, further comprising an immunoglobulin constant domain.

17. An isolated protein comprising a first polypeptide operably linked to a second polypeptide, wherein said first polypeptide comprises a sequence of amino acids of the formula $R1_x$-$R2_y$-$R3_z$, wherein:

R1 comprises a polypeptide of from 100 to 120 residues in length that is at least 90% identical to residues 46-163 of SEQ ID NO:2, and comprises a sequence motif C[KR]Y[DNE][WYF]X{11,15}G[KR][WYF]C (SEQ ID NO:4) corresponding to residues 104-124 of SEQ ID NO:2;

R2 is a polypeptide at least 90% identical to residues 164-234 of SEQ ID NO:2;

R3 is a polypeptide at least 90% identical in amino acid sequence to residues 235-345 of SEQ ID NO:2 and comprises cysteine residues at positions corresponding to residues 250, 280, 284, 296, 335, and 337 of SEQ ID NO:2; a glycine residue at a position corresponding to residue 282 of SEQ ID NO:2; and a sequence motif CX{25,33}CXGXCX{10,33}CX{20,40}CXC (SEQ ID NO:3) corresponding to residues 250-337 of SEQ ID NO:2; and

each of x, y, and z is individually 0 or 1, subject to the limitations that:

at least one of x and z is 1; and

if x and z are each 1, then y is 1;

and wherein said protein modulates cell proliferation, differentiation, metabolism, or migration.

18. The isolated protein of claim 17 wherein said protein is a heterodimer.

19. The isolated protein of claim 18 wherein z is 1 and said second polypeptide is selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, PlGF, PDGF-A, and PDGF-B.

20. The isolated protein of claim 17 wherein said protein is a homodimer.

21. The isolated protein of claim 20 wherein z=1.

22. The isolated protein according to claim 21 wherein each of said first and second polypeptides comprises residues 235-345 of SEQ ID NO:2.

23. The isolated protein of claim 20 wherein x=1.

24. The isolated protein of claim 23 wherein each of said first and second polypeptides comprises residues 46-163 of SEQ ID NO:2.

25. An isolated polynucleotide of up to approximately 4 kb in length, wherein said polynucleotide encodes a polypeptide comprising a sequence of amino acids of the formula $R1_x$-$R2_y$-$R3_z$, wherein:

R1 comprises a polypeptide of from 100 to 120 residues in length that is at least 90% identical to residues 46-163 of SEQ ID NO:2, and comprises a sequence motif C[KR]Y[DNE][WYF]X{11,15}G[KR][WYF]C (SEQ ID NO:4) corresponding to residues 104-124 of SEQ ID NO:2;

R2 is a polypeptide at least 90% identical to residues 164-234 of SEQ ID NO:2;

R3 is a polypeptide at least 90% identical in amino acid sequence to residues 235-345 of SEQ ID NO:2 and comprises

cysteine residues at positions corresponding to residues 250, 280, 284, 296, 335, and 337 of SEQ ID NO:2; a glycine residue at a position corresponding to residue 282 of SEQ ID NO:2; and a sequence motif CX{25,33}CXGXCX{10,33}CX{20,40}CXC (SEQ ID NO:3) corresponding to residues 250-337 of SEQ ID NO:2; and

each of x, y, and z is individually 0 or 1, subject to the limitations that:

at least one of x and z is 1; and

if x and z are each 1, then y is 1.

26. The polynucleotide of claim 25, wherein said polynucleotide is DNA.

27. The polynucleotide of claim 26 comprising nucleotides 1 through 1035 of SEQ ID NO:6.

28. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA polynucleotide accoding to claim 26; and

a transcription terminator.

29. The expression vector of claim 28, further comprising a secretory signal sequence operably linked to the DNA polynucleotide.

30. A cultured cell into which has been introduced an expression vector according to claim 28, wherein said cell expresses the polypeptide encoded by the DNA segment.

31. A composition comprising a protein according to claim 17 in combination with a pharmaceutically acceptable vehicle.

32. A method of producing a protein comprising:

culturing a cell into which has been introduced an expression vector according to claim 28, whereby said cell expresses the polypeptide encoded by the DNA segment; and

recovering the expressed protein.

33. An antibody that specifically binds to an epitope of a polypeptide according to claim 3.

34. The antibody of claim 33 which is a monoclonal antibody.

35. The antibody of claim 33 which is a single-chain antibody.

36. The antibody of claim 33 operably linked to a reporter molecule.

37. A method for detecting a genetic abnormality in a patient, comprising:

obtaining a genetic sample from a patient;

incubating the genetic sample with a polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of SEQ ID NO:1, under conditions wherein said polynucleotide will hybridize to complementary polynucleotide sequence, to produce a first reaction product; and

comparing said first reaction product to a control reaction product, wherein a difference between said first reaction product and said control reaction product is indicative of a genetic abnormality in the patient.

38. A method of stimulating the growth of fibroblasts or smooth muscle cells comprising applying to said cells an effective amount of a protein of claim 17.

39. A method of activating a cell-surface PDGF alpha receptor, comprising exposing a cell comprising a cell-

surface PDGF alpha receptor to the protein of claim 17, whereby the protein binds to and activates the receptor.

40. A method of inhibiting a PDGF alpha receptor-mediated cellular process, comprising exposing a cell comprising a cell-surface PDGF alpha receptor to a compound that inhibits binding of the protein of claim 17 to the receptor.

41. A method of inhibiting zvegf3 activity in a mammal comprising administering to the mammal an effective amount of a zvegf3 antagonist.

42. The method of claim 41 wherein the antagonist is an antibody, a receptor, a ligand-binding receptor fragment, or a receptor IgG-Fc fusion protein.

43. An isolated, antisense polynucleotide that is the complement of the isolated polynucleotide of claim 25.

44. The antisense polynucleotide of claim 43 further comprising operably linked transcription promoter and terminator sequences.

45. A method of inhibiting zvegf3 production in a cell comprising administering to the cell the antisense polynucleotide of claim 44.

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